

Publication

Antiadhesive natural products against uropathogenic E. coli: What can we learn from cranberry extract?

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Extracts from Cranberry fruits (*Vaccinium macrocarpon*) are traditionally used against urinary tract infections, mainly due to antiadhesive activity against uropathogenic E. coli (UPEC), but the exact mode of action and compounds, responsible for the activity, are unknown.; i. To investigate if cranberry extract acts only by a single component or must be assessed as a multi-active-compound preparation; ii to screen isolated cranberry-related natural products under in vitro conditions to pinpoint natural products with antiadhesive effects against UPEC, followed by in silico calculations (QSAR) to predict potential antiadhesive compounds; iii. investigations by using urine samples from cranberry treated volunteers for evaluation on the bacterial transcriptome and the mannose-binding side of FimH, iv. to investigate if besides Tamm Horsfall Protein induction in the kidney, the extract acts also directly against UPEC.; Antiadhesive activity of 105 compounds was determined by flow cytometric adhesion assay (UPEC UT189 on T24 bladder cells). Urine samples from 16 volunteers treated with cranberry extract (p.o., 7 days, 900 mg/day) were used for ex vivo testing concerning influence on the bacterial transcriptome (Illumina RNA-seq) and interaction with the mannose binding domain of type-1 fimbriae.; i. The antiadhesive effect of cranberry extract cannot be attributed to a single compound or to a single fraction. ii. Unglycosylated flavones and flavonols with bulky substitution of the B ring contribute to the antiadhesive activity. 3'-8''-biflavones and flavolignans (not related to cranberry fruits) were identified as potent antiadhesive compounds against UPEC. iii. QSAR yielded a model with good statistical performance and sufficient internal and external predictive ability. iv. Urine samples from male cranberry-treated volunteers indicated significant interaction with the mannose binding domain of type-1 fimbriae, which correlated with the amount of Tamm-Horsfall Protein in the test samples. v Cranberry extract did not influence the UPEC transcriptome; gene expression of bacterial adhesins (P-, S-fimbriae, curli) was not influenced by the urine samples, while a slight, but non-significant upregulation of type 1 fimbriae was observed.; B-ring substituted flavones and flavonols from cranberry contribute to the antiadhesive activity against UPEC by inhibition of the FimH-mediated interaction with the host cell bladder epithelium.

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